PRM250

PATHWAYS OF IMPLEMENTATION OF MULTI-CRITERIA DECISION ANALYSIS INTO ORPHAN DRUG APPROVAL PROCEDURE FOR DRUG SUPPLY PROGRAMS IN RUSSIAN FEDERATION

Serpik VG[1], Yagudina RI[2]
[1]*National Research Institute of Public Health, Moscow, Russia,* [2]*First Moscow State Medical University named after I. M. Sechenov, Moscow, Russia*

BACKGROUND: While the orphan drug supply program is in progress, development of decision-making rules for approving orphan drug for supply program of Russian Federation becomes very actual. Real world data provides evidence, that routine approaches for approving such kind of drugs, e.i. pharmacoeconomic conclusions, are not applicable. Than the need in more appropriate approaches is existed. Multi-criteria decision analysis is one such approaches (MCDA). **OBJECTIVE:** To evaluate prospective of implementation of MCDA in health care system of Russian Federation and to develop road map of MCDA in Russia. **METHODS:** Literature review, cluster analysis, interviewing experts. **RESULTS:** The first step (qualitive) to implement MCDA is to test various MCDA methods to find out optimal one for Russian Federation: it is expected to select the most relevant criteria from the wide range of them. First of all, MCDA is considered to be the instrument to improve the quality of discussion and its transparency, to underline different point of view and unmet needs. On the second stage it may be possible to use quantity MCDA assessment as a rule to approve orphan drugs for drug supply programs. Local recommendations for MCDA in Russian Federation has been published. **CONCLUSION:** Implementation of MCDA as assisting instrument for orphan drug approving for drug supply programs is likely to be a valuable approach, that may improve the quality, transparency of decision-making process and to provide social equity for accepting decisions.

PRM251

PROPENSITY SCORE MATCHING AND SUBCLASSIFICATION WITH MULTI-LEVEL TREATMENTS

Kadziola Z[1], Yang S[2], Imbens GW[3], Cui Z[4], Faries DE[4]
[1]*Eli Lilly Regional Operations GmbH, Vienna, Austria,* [2]*Harvard School of Public Health, Boston, MA, USA,* [3]*Graduate School of Business, Stanford University, and NBER, Stanford, CA, USA,,* [4]*Eli Lilly and Company, Indianapolis, IN, USA*

There is extensive literature on methods, such as propensity scoring, for estimating the causal effects for two treatments using real world data. Much less work has been done for the more general setting with three or more treatments. Whereas the literature has suggested that these propensity-based methods do not naturally extend to the multi-level treatment case, we show, using the concept of weak unconfoundedness, that adjusting for or matching on a scalar function of the covariates removes biases associated with observed covariates. We focused on subclassification and matching approaches as these have found to be effective for two treatments and are among the most popular methods in that setting. We apply the proposed methods to an analysis of the effectiveness of treatments for fibromyalgia from a prospective observational study. We also carried out a simulation study to assess the performance of those new methods relative to such approaches like: pairwise propensity score matching; matching on the Mahalanobis distance of all covariates; matching on the set of propensity scores (with the number of scores equal to the number of distinct treatment levels minus one (Rassen, 2013)); weighting on the inverse of the binary treatment propensity scores (McCaffrey, 2013). The simulations suggest that the proposed methods are simple and viable options for comparing the effectiveness of three or more treatments. RASSEN et al.: Matching by propensity score in cohort studies with three treatment groups. Epidemiology 24, 401–9. MCCAFFREY et al.: A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat. Med. 32,3388–414.

PRM252

GETTING TO REIMBURSEMENT FASTER: COMBINING RANDOMISED, PRAGMATIC, AND OBSERVATIONAL CLINICAL TRIAL DATA

Alsop J
Numerus Ltd, Wokingham, UK

Reimbursement authorities often require pharmaceutical companies to provide them with more than just placebo-controlled data from RCTs. Instead, they typically seek data from a wider "real-world" setting, where the focus is on generating evidence of comparative effectiveness. The natural temptation for many pharmaceutical companies is to provide this evidence from separate, post-market approval studies. However, this approach can be expensive and undoubtedly leads to delays in reimbursement. We propose that both the additional costs of evidence gathering and the delays between regulatory and reimbursement approvals could be reduced by combining the main design elements of randomised, pragmatic, and prospective observational studies into a single, integrated Phase 3/4 study. This single study approach would typically begin with a standard RCT phase where, for example, an initial cohort of patients would be randomised to receive either the investigational therapy or placebo. Either in parallel with or following this phase, a second patient cohort would be randomised under pragmatic clinical trial conditions with the aim of comparing the investigational therapy with placebo and a limited number of active comparator treatments. Lastly, a third (observational) cohort would be enrolled and allocated to a wider range of therapies, as per clinical practice. Data from the RCT cohort would be used to obtain limited regulatory approval. Following this, data from the pragmatic cohort, once available, would then be formally combined using standard statistical techniques with data from the RCT cohort in order to obtain a wider regulatory approval and possibly some form of conditional reimbursement. The pragmatic and observational cohorts would then provide the comparative effectiveness data to allow for reimbursement across different patient groups. We outline the strengths and weaknesses of this approach, and discuss its operational considerations.

PRM253

AN EPIDEMIOLOGIC MODELING APPLICATION TO PHARMACOECONOMICS FOR IMPROVED HEALTH CARE PLANNING

Cid Ruzafa J, Cox A, Merinopoulou E, Baggaley R, Leighton P, Desai K
Evidera, London, UK

Epidemiologic and pharmacoeconomic models differ in terms of populations considered, mathematical techniques used, and questions addressed. A typical pharmacoeconomic model assesses chronic or acute conditions, uses Markov techniques, and considers a closed patient group receiving a defined therapy to assess incremental costs needed to achieve gains in quality adjusted life years. A typical epidemiologic model assesses vaccination or public health interventions for infectious disease using differential equations and considers open populations representing communities to estimate prevalence or numbers of disease cases averted. The manner of conducting sensitivity analyses also differs. In oncology, in which multiple lines of treatment are available, the epidemiologic approach has application to estimate the patient point prevalence or the number of patients who can start on a line of therapy over a certain time period, when this cannot be determined from clinical trials or registers (which usually focus on single lines of therapy or limited types of patients that are not representative of the overall patient population). The approach consists of conceptualizing an open population that incorporates incidence of the condition and the transition of patients through various lines of treatment until death, and uses systems of difference/differential equations. Parameterization is challenging if there are several prognostic factors to describe the patient population, multiple or complex treatment pathways, and a wide range of variability. Parameters are obtained from the published literature, analyses of database information, and/or surveys to experts in the field. Steady state solutions of the model equations estimate point and period prevalence. This approach is applicable to gastrointestinal stromal tumours and multiple myeloma. Resulting estimates are important for budget impact analysis and health care services planning by reducing uncertainty associated with identifying the patient numbers eligible for a given treatment. Epidemiologic modelling permits a framework to estimate disease prevalence that is little used in pharmacoeconomics.

PRM254

NON-INTERVENTIONAL RESEARCH ETHICAL REQUIREMENTS IN ENGLAND AND FRANCE: SHARED EXPERIENCE FROM A BINATIONAL RESEARCH PROJECT

Guillemot J, Boval MC, Gauthier A
Amaris, London, UK

BACKGROUND: Ethical review for non-interventional research is progressively becoming part of research standards. This evolution ensures that participants in research are respectfully considered. In practice, information on ethical requirements for non-interventional research seems insufficient. Increasing and legitimate expectations from peer-reviewed journals regarding reviews by ethics committees sometimes challenge researchers. In this presentation, we share our experience of investigating ethical requirements for conducting a questionnaire-based research on physicians in France and England. **METHODS:** This investigation consisted of a documentary analysis, including official guidance documents on ethical requirements, communications with institutions and publications reviews. Documents were identified using an ad hoc search on official websites. Publications were identified on PubMed. **FINDINGS:** In England, the service of the National Research Ethics Service (NRES) serves as the ethics reviewer. It offers an informal preliminary review of the study protocol and estimates ethical risks associated with non-interventional research projects. Depending of the target population, the methods and the risk level associated with the research project, the NRES states whether a formal ethics application is necessary or not. In case of low risk projects the NRES supplies an email which can be used as a justification for peer-reviewed journals. In France, structures to support ethical reviews for non-interventional research are the result of an on-going reform. *Comités de Protection de la Personne*, or CPPs, fulfil the role of ethics reviewers although they were initially designed to collaborate for hospital-based research. Gaining ethical review in France was more complex due to the infrequent character of such request from the industry. **CONCLUSION:** This experience showed the increasing role of ethical requirements in non-interventional research. It is a domain in constant movement which calls for innovative approaches to compile and disseminate information regarding ethical requirements for non-interventional research across Europe and the world, especially regarding cross-national research projects.

PRM255

REAL WORLD STUDIES, CHALLENGES, NEEDS AND TRENDS FROM THE INDUSTRY

Batrouni M, Comet D, Meunier JP
Axonal, Paris, France

OBJECTIVES: To understand key challenges, needs and trends for conducting real world studies (RWS). **METHODS:** An online survey conducted in September 2013 within key players in the pharmaceutical and medical device industry in EU and US. 456 persons have been solicited through emails and phone calls, 107 have responded to the questionnaire. Respondents were mostly occupying senior positions in medical affairs, health economics and outcome research. **RESULTS:** 27% RWS conducted are requested by Health Authorities, 73% on the industry initiative. 75% of those studies are subcontracted to a CRO. The main criteria of choice are the experience in RWS, particularly in the regulation process, the capacity to deliver on time and a flexible and adaptable structure. The RWS activity is expected to increase by 25 % in the next two years. Most of those studies have safety and effectiveness objectives and to a lesser extent drug utilization and health economics and the most common therapeutic areas are: oncology, cardiovascular and metabolic disorders. In addition, pharmaceutical companies are conducting more and more epidemiological studies to prepare dossiers for market access (disease understanding, unmet needs, population targeting). **CONCLUSION:** The pharmaceutical market is becoming global and is expanding into new countries and therapeutic areas. The result is an increase in the need for RWS where the regulatory agencies are asking for additional data